

KINETIC TRAPPING OF METASTABLE AMINO ACID POLYMORPHS

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Second harmonic generation (SHG) microscopy was integrated with synchrotron X-ray diffraction (XRD) to test the Ostwald Rule of Stages, in which is hypothesized that crystals dynamically transition through metastable polymorphs before settling on the most thermodynamically favored form. The presence or absence of metastable forms has historically been challenging to probe due to the stochastic randomness of crystal nucleation coupled with the relatively short time-frame over which the metastable forms may survive. In this work, inkjet printing of a racemic amino acid solutions results in rapid solvent evaporation, placing crystallization under kinetic rather than thermodynamic control. SHG microscopy is used to rapidly and selectively identify the positions of metastable crystal forms. Coupling this measurement with synchrotron XRD allows diffraction analysis to be performed on individual inkjet printed dots of only a few pg of total material, prepared from single 1 pL droplets. In studies of amino acids, we have shown that the homochiral crystals emerge when printed, while those same solutions exclusively generate the racemic co-crystals upon slow solvent evaporation.